

A MATHEMATICAL MODEL OF CARDIOVASCULAR RESPONSE TO DYNAMIC EXERCISE

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Abstract—A mathematical model of cardiovascular response to dynamic exercise is presented. The model includes the pulsating heart, the systemic and pulmonary circulation, a functional description of muscle exercise hyperemia, the mechanical effects of muscle contractions on hemodynamics, and various neural regulatory mechanisms working on systemic resistance, venous unstressed volume, heart rate and ventricle contractility. These mechanisms comprehend the direct effect of motor command signals on cardiovascular and respiratory control centers (the so called central command), arterial baroreflex and the lung-stretch receptor reflex. The model is used to simulate the steady state response of the main cardiovascular hemodynamic quantities (systemic arterial pressure, heart rate, cardiac output, systemic vascular conductance, and blood flow in working muscle) to various intensity levels of two-legs dynamic exercise. A good agreement with physiological data in the literature has been obtained. The model sustains the hypothesis that motor command signals emanating from cerebral cortex provide the primary drive for changes of circulation and respiration during exercise. The model may represent an important tool to improve understanding of exercise physiology.

Keywords - Dynamic exercise, central command, autonomic nervous system

I. INTRODUCTION

Physical activity, among other various stresses encountered in normal life, mostly challenges the regulatory abilities of the cardiorespiratory system. During exercise, the cardiovascular and respiratory systems must act in concert in order to supply adequate oxygen and nutrients to working muscles, sustain removal of carbon dioxide and other metabolic products, dissipate heat and, at the same time, maintain the requirements of other essential organs. To achieve this, dynamic exercise is accompanied by hyperpnea, increase in cardiac output, and redistribution of blood flow towards active muscles, mainly due to a strong decrease in their vascular resistance. As a consequence of skeletal muscle vasodilation, total peripheral resistance falls and mean arterial pressure only rises modestly. These cardiovascular adjustments result from a superimposition between extravascular mechanical effects of muscle contraction (the so called muscle pump), local vascular control processes and a reconfiguration of autonomic nervous activity: in particular, sympathetic activity to heart and vessels increases, while cardiac vagal tone withdraws.

Even if this scenario is amply documented [1-4], a clear comprehension of the underlying mechanisms is still lacking. In particular, the origin of the readjustment of the autonomic nervous system, as well as the origin of respiratory response have not been established yet and various hypotheses exist. Several experimental results [5-7] support the idea that changes in ventilation and in cardiovascular variables which

occur during exercise, may be partly due to an “irradiation” of motor impulses descending from cerebral cortex into cardiovascular and respiratory control areas. This idea is known as “central command” hypothesis, and presumes that no signals are fed back from the periphery to the center (i.e., a feed-forward controller). Feedback control mechanisms originating in working muscle have been proposed to contribute to exercise response, too [8,9]. Nevertheless, the role of muscle afferents during actual dynamic exercise is strongly controversial, especially in human subjects [3]. Finally, feedback from central and peripheral chemoreceptors could not be implicated in the respiratory response, since arterial gas levels only show little changes [6,7]. The complexity of the problem is further increased since changes in cardiorespiratory variables evoked by exercise may elicit the secondary action of additional control mechanisms (such as baroreceptors or receptors located in the lungs).

Aim of this work is to present a mathematical model of the cardiovascular regulation to dynamic exercise, with particular emphasis given to the role of central command. In the model central command is a function of relative intensity of exercise, and directly affects autonomic nervous activity and respiration. Furthermore, the model includes a description of the local metabolic mechanisms involved in muscle exercise hyperemia and the muscle pump. Finally, all these mechanisms interact with the baroreflex system and with the lung-stretch receptor reflex.

II. METHODOLOGY

In the following, a qualitative description of the mathematical model is presented.

The model distinguishes between the controlled system (i.e.: the heart and the vascular system) and the control mechanisms.

A. Plant

Fig. 1 shows the electric analog of the cardiovascular system. The pulmonary circulation includes 3 compartments, differentiating among large arteries (subscript “pa”), peripheral (“pp”) and venous (“pv”) circulation. The systemic circulation includes 13 compartments. The first represents the large systemic arteries (“sa”). The others describe the peripheral and venous circulation in six districts arranged in parallel: brain, heart, active muscle, non active or resting muscle, splanchnic circulation and the remaining extrasplanchnic vascular beds (subscripts “b”, “h”, “am”, “rm”, “s” and “e”, respectively). A distinction among these regions is necessary since regulatory mechanisms exert a different action on each of them [10]. The active muscle

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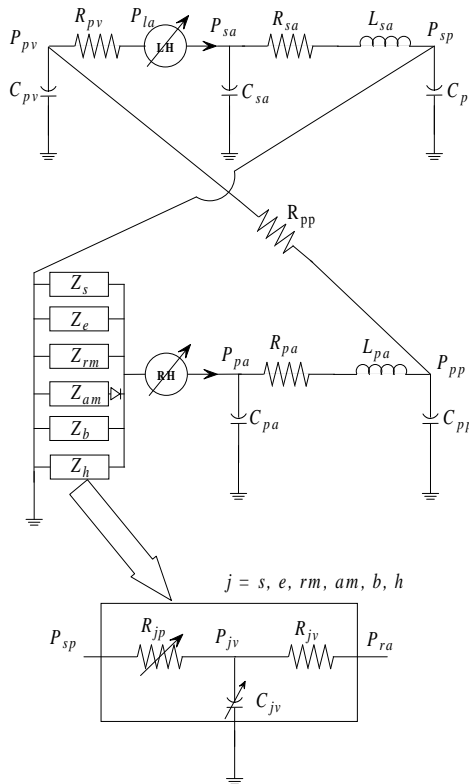


Fig.1. Electric analog of the cardiovascular system. See text for symbol meaning. The ideal diode between Ramv and the right heart mimics the venous valves in active muscle compartment, which prevent retrograde flow. $C_p = C_{sp} + C_{cp} + C_{rm} + C_{am} + C_{bp} + C_{hp}$.

branch mimics skeletal muscle in the legs, since in this work we simulated the response to two-legs exercise. Hemodynamic in each compartment is reproduced by means of a hydraulic resistance (“R”) and a linear pressure-volume curve, characterized by an unstressed volume and a constant compliance (“C”). The only exception is the venous active muscle compartment (“mav”), where we used a non linear relationship between blood volume and transmural pressure [11], in order to obtain a more reliable description of muscle pump. Mechanical effects of muscle contractions have been simulated assuming that extravascular pressure outside active muscle veins (i. e., intramuscular pressure) changes periodically during exercise [12]. Finally, the inertial effects have been included only in the large artery compartments (inertances L_{sa} and L_{pa}), where blood acceleration is significant. The heart embodies passive atria (subscripts “ra” and “la”), described through a linear capacity, and pulsating ventricles (“rv” and “lv”), simulated by a time-varying elastance model.

B. Control mechanisms

In the description of the control system, a distinction is made between afferent pathways, which carry signals from periphery to the central neural system, the efferent sympathetic and parasympathetic pathways and the action of several distinct effectors (Fig. 2).

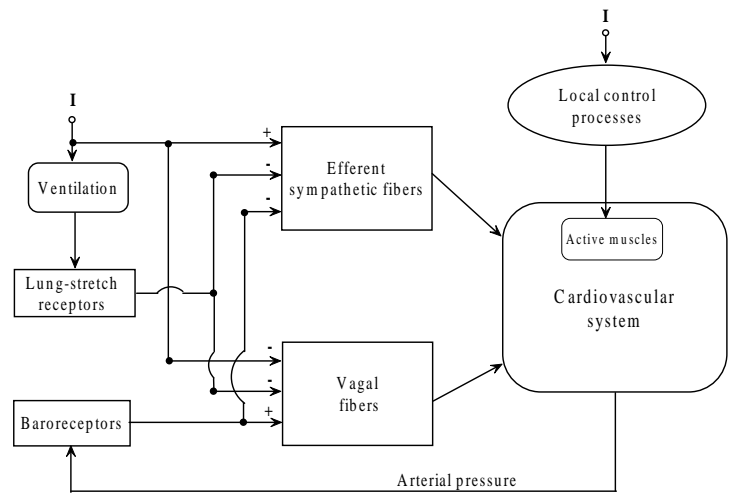


Fig. 2. Block diagram of control mechanisms. I = exercise intensity.

The afferent pathways transport information from arterial baroreceptors and from lung-stretch receptors. The arterial baroreceptors respond to changes in both the instant value of systemic arterial pressure and its rate of change [13]. Slowly adapting lung-stretch receptors respond to changes in tidal volume [14]. Each afferent mechanism is mimicked through a static characteristic and a first order dynamic.

The efferent pathways embrace four different kinds of fibers: sympathetic fibers to systemic arterioles, sympathetic fibers to the veins, sympathetic fibers to the heart, and the vagus. The activity in these fibers is a non-linear monotonic function of the weighted sum of afferent information, where weights may be positive or negative. Moreover, sympathetic and parasympathetic activities are influenced by the central command, too. According to experimental results [3,4], central command has an inhibitory effect on the vagus, while excites sympathetic activities. The relationships between the central command and the efferent activities are monotonic functions of the relative exercise intensity with a lower threshold and an upper saturation level.

The effectors include the response of systemic peripheral resistance and venous unstressed volume (in the splanchnic, active and non-active muscle, and other extrasplanchnic compartments) to activation of sympathetic fibers, the response of heart contractility to cardiac sympathetic nerves, and the response of heart period to cardiac sympathetic nerves and to the vagus. Each effector response comprehends a pure delay, a monotonic static function and a first-order low-pass dynamic. In order to reproduce muscle exercise hyperemia, we assumed that peripheral resistance in the active muscle compartment (R_{amp}) depends not only on neural influences, but also on local metabolic control mechanisms. The latter comprise the effect of increased oxygen consumption rate and of metabolic production of vasodilator substances [2,12], each described as a function of exercise intensity through a static characteristic and a first-order low-pass dynamics. Both an increase of O_2 consumption over the basal level and the release of vasodilator substances produce a decrease in R_{amp} . Finally, in the model the activity of lung stretch receptors is a function

of changes in tidal volume. According to experimental results [1], we assumed that tidal volume in static conditions is a linear function of exercise intensity. This function mimics the drive of the central command on respiratory control centers.

All functions and parameters in the model have been taken from the physiological literature. The model has been simulated on a personal computer with Pentium processor, by using the Runge-Kutta-Fehlberg 4/5 algorithm with adjustable step length for the numerical integration of ordinary differential equations.

III. RESULTS

Validation of the model has been achieved simulating cardiovascular response to different levels of dynamic exercise in steady state conditions, and comparing simulation results with clinical and physiological data. The only input for the model is the relative intensity of aerobic exercise (I). At rest I is equal to 0, while at the anaerobic threshold I is conventionally set equal to 1.

Fig. 3 compares the percentage changes in heart rate (HR), cardiac output (CO), mean systemic arterial pressure (MAP), systemic vascular conductance (SVC), and blood flow in active muscles (Q_{am}) computed with the model at four different exercise levels, with analogous data in humans [2]. As it is clear from the figure, the agreement between simulation and in vivo results is satisfactory.

Fig. 4 shows the distribution of cardiac output between the different organs obtained with the model at the same exercise intensities considered in Fig. 3. The model is able to reproduce the redistribution of blood flow towards working muscle during exercise, amply documented in physiological literature [3,4].

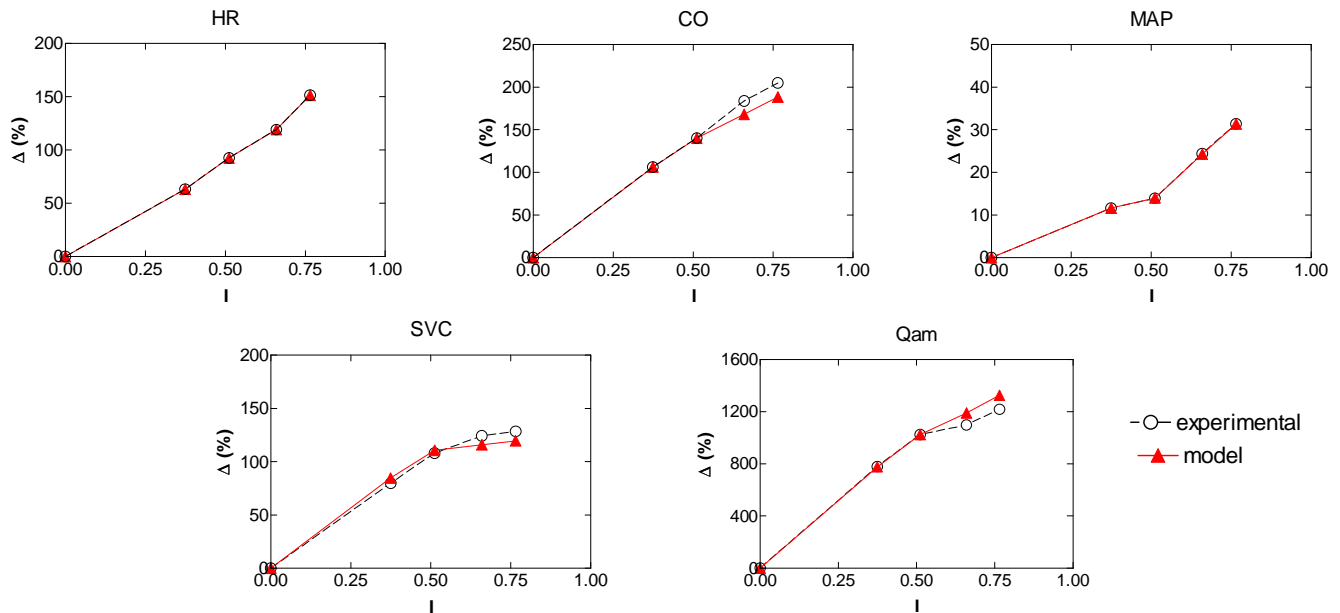


Fig. 3. Percentage changes in heart rate (HR), cardiac output (CO), mean arterial pressure (MAP), systemic vascular conductance (SVC), and blood flow in active muscles (Q_{am}) plotted versus relative exercise intensity (I). Closed red symbols connected by solid line are model results; open black circles connected by dashed line are experimental data on human subjects [2].

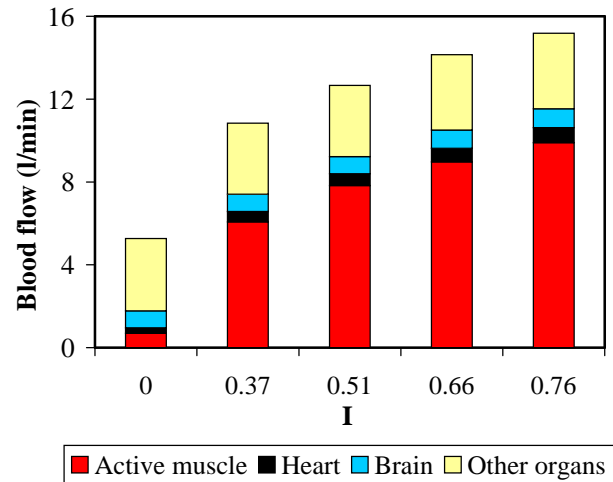


Fig. 4. Distribution of cardiac output between different organs obtained with the model at the same four exercise intensities considered in Fig. 3.

IV. DISCUSSION

As it is clear from Figs. 3 and 4, the main cardiorespiratory effects of exercise aim to supplying adequate oxygen and nutrients to working muscles. Model ascribes these adjustments to the complex interaction among local metabolic control processes, mechanical effects of muscle contractions, the action of central command and activation of reflex mechanisms, secondary to changes in cardiorespiratory variables directly elicited by exercise. In particular, in the model a primary role is played by the central command, which exerts its action both on vagal and sympathetic fibers. Its effect on efferent activities may be briefly summarized as follows. Action of central command on vagus reaches its

maximal strengthen at very low exercise intensity, causing vagal activity to fall near 0. On the contrary, central command starts to affect sympathetic activity to heart only when exercise intensity is moderate (I near 0.4), then it rises rapidly. This is consistent with experimental evidences [3]. Activity in the sympathetic fibers to veins starts to increase at low exercise intensities and rapidly reaches an high saturation level. Finally, action of central command on sympathetic fibers to peripheral resistances is null at low exercise intensities, then it increases modestly.

In the model, the primary changes in autonomic nervous activity elicited by central command are modulated by activation of secondary reflex mechanisms. In particular, increase in arterial pressure triggers the baroreflex system, causing a decrease in sympathetic activities and an increase in the vagal one, while the increase in tidal volume elicits lung-stretch receptors which induce a decrease in sympathetic activity to vessels and in vagal activity, too. Thus the value of efferent activities during exercise results from the interaction between several components, in part excitatory, in part inhibitory, which superimpose non-linearly. Finally, interaction between neural influences and local processes determines the final response of the hemodynamic quantities. In particular, in active muscle local vasodilator mechanisms predominates on neural influences, causing a fall in R_{amp} and thus a strong increase in Q_{am} . It is worth noting that blood flow in other organs remains practically unchanged, since antagonist effects on these organs (vasoconstriction, increasing in MAP) tend to balance each other.

V. CONCLUSION

In conclusion, the present work is able to integrate the main mechanisms involved in exercise response into a single theoretical framework. The simulation results show that the model is able to reproduce cardiovascular response in a large range of exercise intensity, sustaining the idea that central command is the primary drive for changes in circulation and respiration during exercise. Moreover, the model underlines the extreme complexity of exercise response, resulting from the non-linear interaction of many mechanisms (sometimes synergistic, sometimes antagonistic), simultaneously operating. At present, the model may be useful in the interpretation of experimental and clinical data, to improve our understanding of exercise physiology and as an educational tool to analyze the complexity of cardiovascular and respiratory regulation. In perspective, it may be of clinical value since knowledge of the cardiovascular effects of exercise may be used in diagnosis of disease states.

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